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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/920,394

08/01/2001

Rosanne M. Crooke

ISPH-0589

4398

36441

7590

01/13/2005

EXAMINER

SCHULTZ, JAMES

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ART UNIT

PAPER NUMBER

1635

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/920,394

Applicant(s)

CROOKE ET AL.

Examiner

J. D. Schultz, Ph.D.

Art Unit

1635

-- **Th MAILING DATE of this communication app ars on the cov r sh et with th correspondenc address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 18 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 4-10,12,13,15 and 24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 4-10,12,13,15 and 24 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 5-6-2003.

- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Status of Application/Amendment/Claims***

Applicant's response filed 18 October 2004 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 22 March 2004 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Information Disclosure Statement***

In view of Applicants comments, the reference of Toyama has been considered in full, and a signed copy of the IDS entered May 6, 2003 which lists said reference as cite no. "CB" has been initialed accordingly.

Furthermore, it is noted that applicants filed a new IDS on 27 December 2004. At the time of writing of this action, the IDS and the references filed therewith had not yet been scanned into the Image File Wrapper system and were thus unavailable for review. Because said IDS will be available by the time applicants respond to the present action, consideration of the IDS filed on 27 December 2004 will be addressed in the next Official action.

### ***Response to Claim Rejections - 35 USC § 35 U.S.C. § 103(a)***

Claims 4-10, and 12, 13, 15, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al. (U.S. Patent 5,968,749), or Chang et al. (U.S. Patent 5,484,727),

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in view of Baracchini et al. (U.S. Patent Number 5,801,154) and Taylor et al (Drug Disc. Today, 1999. 4(12) 562-567), and is repeated for the same reasons as set forth in the Office action mailed July 16, 2003.

The arguments provide by applicants have been addressed in the response filed 18 October 2004. However, applicants reiterated arguments are addressed as follows. Applicants traverse the instant rejection by arguing that it is not as easy and straightforward to determine target sites on a gene that permit one to identify suitable antisense oligonucleotides with a high degree of inhibition a priori as indicated by Taylor, because Taylor et al. makes such allegations without providing evidence. Particularly, applicants dispute the statement by Taylor et al that with the use of high affinity oligonucleotides and bioinformatics screening programs, that one of skill need screen only 3-6 oligos to find one that inhibits from 66-95% efficiency.

In disputing this statement of Taylor, applicants have provided a declaration under 37 CFR § 1.132. The declaration includes a statement from a representative of the assignee indicating her belief that it is never possible to predict reliably before the screen is performed, whether one of skill need screen only 3-6 oligos to find one that inhibits from 66-95% efficiency. Applicants submit examples of two genes which were subjected to antisense-inhibition assays using 80 different oligos per gene. Applicants report results whereby no oligo attained more than 50% inhibition against one gene, and 40% against the other.

In response, applicants are reminded that the instantly claimed invention requires oligos that inhibit only to 12% or 30%. Thus, the submission of data showing oligos with 50% inhibition against one gene and 40% against the other would not seem to support the notion that it is difficult to find oligos that inhibit 12% or 30%.

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Furthermore, it is maintained that this submission is not representative of the state of the art of antisense gene inhibition in general. The instant assignee has received over 250 U. S. Patents with the terms "antisense" in the claims. A review of 10 randomly selected patents reveals that all 10 have many oligos in each that inhibit above the 12% mark, with a significant number over 30%. For example, table 1 of U. S. Patent Number 6,001,992 (col. 27) contains tests results for 15 oligos, with 4 of the 15 exhibiting over 60% inhibition. Thus, the inventors of this patent found 1 oligo exhibiting 60% inhibition for every 3.6 screened, well within the range indicated by Taylor et al. A table from another randomly selected different patent, U. S. Patent Number 6,312,900 (col. 21) returned a much higher number of hits, whereby 7 out of 10 oligos tested achieved inhibition of at least 60%. This is 1 oligo for every 1.4 tested that achieve said level of inhibition (both patents are of record). Thus, a strong case can thus be made that applicants' submitted data may not be representative of every instance of antisense oligonucleotide mediated gene inhibition.

Applicants have also failed to indicate whether high affinity chimeras were used in their data submitted under 37 CFR 1.132, and are thus related to the screening method referred to by Taylor. While applicants have certainly used chimeric oligos comprising DNA and RNA in their specification, these do not appear to be high affinity chimeras, that is those that contain modifications designed to increase hybridization affinity. Applicants have not indicated either way what their conditions are relative to the teachings of Taylor et al., and thus it is not clear how such evidence is related to the teachings of Taylor.

Finally applicants allege that one skilled in the art could not expect, prior to screening, that an antisense oligonucleotide with high inhibitory action against any selected target can be

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identified simply because antisense methodologies are known in general and a gene sequence of the proposed target is published. However, as stated above, this is undermined by applicants' own submission which shows oligos with 50% inhibition against one gene and 40% against the other. This is held to be a considerable level of inhibition. Thus arguments of the declaration are not considered convincing.

Applicants arguments regarding the remainder of the references used in the 35 U.S.C. § 103(a) rejection are not considered convincing, because applicants argue each reference individually. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). It is acknowledged that the references when viewed individually do not teach the presently claimed invention; however, the test for obviousness is what the *combined* teaching of the prior art would have suggested to those of ordinary skill in the art.

Thus, while it is pointed out that Chang *et al.* do not provide specific antisense sequences, they do teach SEQ ID NO: 3 as claimed instantly, and teach that antisense can be used to inhibit SEQ ID NO: 3. Chang was not relied upon for a teaching of specific antisense sequences. Applicants also point to the functional language drawn to the inhibition of "endogenous" ACAT sequences, and suggest that Chang does not teach inhibition of the endogenous sequence. However, such functional language does nothing to limit the structure of the compound to which the claim is drawn (i.e. the antisense oligo), and accordingly is not granted patentable weight. Furthermore, both Baracchini and Taylor are considered to provide information sufficient to

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make, test, and use antisense oligos directed to the instant target. Finally, although Chang *et al.* does not Baracchini *et al.* teaches that the start codon, coding region, and stop codon are preferred targeting regions of a target. Since the instantly recited target is drawn to nucleotides 14-1741 of SEQ ID NO: 3, which corresponds to the start codon through the stop codon and includes the entire coding region, targeting said region is considered to be obvious. The fact that routine screening is required to find some of the oligos does not mean that the invention is merely obvious to try, because one of ordinary skill in the art would have a reasonable expectation of success in using the teachings of the instantly cited art to make and use antisense oligos *in vitro*.

### ***Conclusion***

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz, Ph.D. whose telephone number is 571-272-0763. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

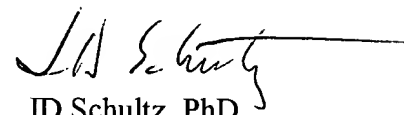
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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JDS



JD Schultz, PhD  
Patent Examiner  
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